

## Metered Dose Inhaler with Spacer in Children with Acute Asthma

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### WHAT IS THE ISSUE?

The 'decision question' is whether metered dose inhaler with spacer should (could) be used for delivery of bronchodilator in children with acute asthma. The 'clinical question' is: "*In children with acute asthma (population), does bronchodilator delivery using metered dose inhaler with spacer (intervention) result in better clinical response (outcome) as compared to delivery with nebulizers (comparison)*"

### EURECA

#### RELEVANCE

Metered dose inhaler (MDI) with spacer has become a preferred modality for delivering preventer (inhaled corticosteroid) therapy in children with persistent asthma. This has virtually replaced the use of oral and parenteral medication in routine home-based management of asthma. During acute exacerbations, physicians tend to use nebulizers for delivery of bronchodilator medication. Some studies suggest that MDI with spacer may also be efficacious(1,2) and recent British Thoracic Society Guidelines favour this mode over nebulizers(3). Potential benefits may be reduction in cost, greater convenience and less incidence of infection. It is therefore pertinent to assess whether MDI with spacers are useful in children with acute asthma episodes. The clinical question as well as the intervention is relevant in clinical practice in the Indian scenario.

#### CURRENT BEST EVIDENCE WITH CRITICAL APPRAISAL

An updated Pubmed search (18 December 2007), with the terms (*acute asthma spacer nebulizer*) and

limits (*Humans, Meta analysis, Randomized Controlled Trial, All Children 0-18 years*) resulted in 39 citations including two systematic reviews(4,5). Data from the latest Cochrane systematic review(4) and two additional randomised controlled trials(6,7) contribute to current best evidence. Five potentially relevant publications could not be included as they were not randomized trials(8-12).

The Cochrane review(4) included 19 trials with over 1200 children (more than two years of age) presenting with acute asthma in the community setting or hospital emergency department. Patients who were already admitted were also included. Thus the participants in the various trials resembled the real-life setting. However, all trials had excluded children with life threatening acute exacerbations; hence the results of the review cannot be directly extrapolated to such children. Each included trial used the same beta-2 agonist, given either by nebulizer or MDI with spacer. As in real life, there was no emphasis on any particular type of nebulizer or spacer. However, the reviewers did not consider a sub-group analysis based on either the absolute dosage of bronchodilator or the ratio of the dose delivered by the two methods.

The systematic review conformed to the usual rigorous methodology for which Cochrane reviews are acclaimed, including independent data extraction by two reviewers, exploration of heterogeneity between trials and sensitivity analysis (excluding trials of lower methodological quality). However, intention to treat analysis was not performed and the impact of subjects, who did not comply with the trial protocols, remains unclear. This is an important issue because reporting of results in only those subjects who complete the protocol can lead to bias.

### EURECA CONCLUSIONS IN THE INDIAN CONTEXT

- In acute asthma, bronchodilator delivery through metered dose inhaler with spacer is comparable, but not superior to nebulizer in terms of clinical response and adverse events.
- These results cannot be directly applied to children less than two years and those with life-threatening acute exacerbations for want of adequate data.
- There is no evidence on the impact of these delivery modes on convenience, incidence of infection and cost of therapy.

The Cochrane review showed that the relative risk of hospitalization in children with acute asthma was not significantly different whether they received bronchodilator through nebulizer or MDI with spacer, suggesting that both delivery routes are equally efficacious in terms of clinical response. Likewise for admitted patients, the duration of hospitalization was similar with both delivery methods. The authors reported that duration of stay in the emergency department was significantly shorter with spacers as compared to nebulizers, but they failed to use a random effects model for this comparison. Our analysis using this method showed that this outcome also was comparable. Other outcomes suggestive of clinical response such as increase in FEV<sub>1</sub> and final increase in PEF following multiple doses of bronchodilator were also comparable in both groups. In terms of adverse events reported, there was more tachycardia with nebulizers (statistically significant difference), suggesting that MDI with spacer may be preferable. However, this result must be interpreted in light of the fact that the absolute difference was not clinically significant; therefore the two delivery options are comparable in this respect. Similarly, the risk of developing tremor appears to be less with MDI and spacer, but data are limited to draw a definite conclusion on this. Change in transcutaneous oxygen saturation also was similar irrespective of the delivery mode.

One of the two additional randomized trials(6) included 90 children and demonstrated compar-ability between both interventions with respect to FEV<sub>1</sub>, oxygen saturation, score for accessory muscle usage, wheezing and dyspnea, using intention to treat analysis. The increase in heart rate was reported to be less with MDI plus spacer. The other trial(7) randomized

79 children and demonstrated compar-able duration of stay in emergency, hospitalization rate, clinical course and relapse rate. Thus these additional trials also reported conclusions in line with the Cochrane review, suggesting that the evidence is robust.

### EXTENDIBILITY

Only two of the 21 trials comprising current best evidence were performed in India, although there were a few more in similar clinical settings. The results of these trials were not very different from those conducted in developed countries or ‘western’ children. Further, there is no reason to believe that Indian children should behave differently either in terms of asthma or response to bronchodilator by the two delivery methods under evaluation. Therefore, the evidence can be extended to our setting.

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### REFERENCES

1. Leversha AM, Campanella SG, Aickin RP, Asher MI. Costs and effectiveness of spacer versus nebulizer in young children with moderate and severe asthma. *J Pediatr* 2000; 136: 497-502.
2. Duarte M, Camargos P. Efficacy and safety of a home-made nonvalved spacer for bronchodilator therapy in acute asthma. *Acta Paediatr* 2002; 91: 909-913.
3. British Thoracic Society. British Guidelines on Asthma Management. *Thorax* 2003; 58 (Suppl 1): i1-i94.

4. Cates CJ, Crilly JA, Rowe BH. Holding chambers (spacers) versus nebulizers for beta-agonist treatment of acute asthma. *Cochrane Database Syst Rev* 2006; 2: CD000052.
  5. Castro-Rodriguez JA, Rodrigo GJ. Beta-agonists through metered-dose inhaler with valved holding chamber versus nebulizer for acute exacerbation of wheezing or asthma in children under 5 years of age: a systematic review with meta-analysis. *J Pediatr* 2004; 145: 172-177.
  6. Schuh S, Johnson DW, Stephens D, Callahan S, Winders P, Canny GJ. Comparison of albuterol delivered by a metered dose inhaler with a spacer versus a nebulizer in children with mild acute asthma. *J Pediatr* 1999; 135: 22-27.
  7. Sannier N, Tismit S, Cojocar B, Leis A, Wille C, Garel D, *et al.* Metered dose inhaler with spacer vs. nebulization for severe and potentially severe acute asthma treatment in the pediatric emergency department. *Arch Pediatr* 2006; 13: 238-244.
  8. Jamalvi SW, Raza SJ, Naz F, Shamim S, Jamalvi SM. Management of acute asthma in children using metered dose inhaler and small volume nebulizer. *J Pak Med Assoc* 2006; 56: 595-599.
  9. Benito Fernandez J, Trebolazabala Quirante N, Landa Garriz M, Mintegi Raso S, Gonzalez Dias C. Bronchodilators via metered-dose inhaler with spacer in the pediatric emergency department: what is the dosage? *An Pediatr (Barc)* 2006; 64: 46-51.
  10. Cates C. Spacers and nebulizers for the delivery of beta-agonists in non-life-threatening acute asthma. *Respir Med* 2003; 97: 762-769.
  11. Mandelberg A, Tsechori S, Hourri S, Gliad E, Morag B, Priel IE. Is nebulized treatment necessary in the pediatric emergency department? *Chest* 2000; 117: 1309-1313.
  12. Horner SD. A low dose of albuterol by metered-dose inhaler with a spacer was as effective as higher doses by metered-dose inhaler or low doses by nebulizer in children with mild acute asthma. *West J Med* 2000; 172: 247.
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